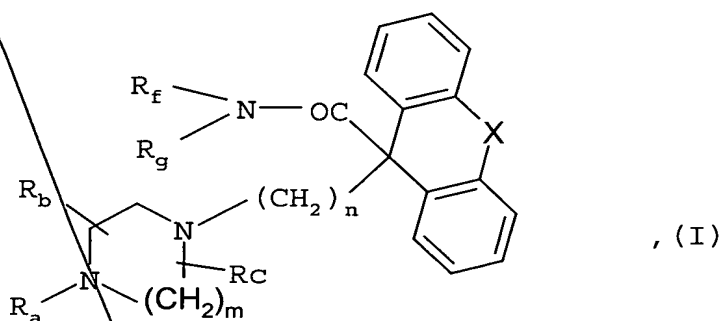


Patent Claims

1. Substituted piperazine derivatives of general formula



wherein

n denotes the number 1, 2, 3, 4 or 5,

m denotes the number 2 or 3,

X denotes a carbon-carbon bond, an oxygen atom, a methylene, ethylene, imino or N-(C₁₋₃-alkyl)-imino group,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R₁ and R₂, wherein

R₁ denotes a hydrogen, fluorine, chlorine or bromine atom, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a hydroxy group, a C₁₋₄-alkoxy group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a phenoxy, heteroaryloxy, phenyl-C₁₋₃-alkoxy, carboxy, C₁₋₃-alkoxycarbonyl, aminocarbonyl, C₁₋₃-alkylaminocarbonyl, N,N-di-(C₁₋₃-alkyl)-aminocarbonyl, nitro, amino,

C_{1-3} -alkylamino, di- $(C_{1-3}$ -alkyl)-amino, phenyl- C_{1-3} -alkyl-amino, N- $(C_{1-3}$ -alkyl)-phenyl- C_{1-3} -alkylamino, C_{1-3} -alkylcarbonylamino, N- $(C_{1-3}$ -alkyl)- C_{1-3} -alkylcarbonylamino, C_{1-3} -alkylsulphonylamino or N- $(C_{1-3}$ -alkyl)- C_{1-3} -alkylsulphonylamino group, while the abovementioned phenyl or heteroaryl moieties of the group R_1 may be substituted by one to five fluorine, chlorine or bromine atoms, a C_{1-3} -alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a hydroxy group, or a C_{1-4} -alkoxy group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, and

R_2 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3} -alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or a C_{1-4} -alkoxy group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or

R_1 and R_2 together represent a methylenedioxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl or monocyclic heteroaryl group, while the abovementioned phenyl groups and heteroaryl groups may in each case be substituted by a fluorine, chlorine or bromine atom, a C_{1-3} -alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, by a hydroxy, C_{1-3} -alkoxy, carboxy, C_{1-3} -alkoxycarbonyl, aminocarbonyl, C_{1-3} -alkylaminocarbonyl or N,N-di- $(C_{1-3}$ -alkyl)-aminocarbonyl group,

R_b and R_c independently of one another denote a hydrogen atom or a C_{1-3} -alkyl group and

R_f and R_g , which may be identical or different, denote hydrogen atoms, C_{1-6} -alkyl groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, C_{3-7} -cycloalkyl groups, phenyl, heteroaryl, phenyl- C_{1-3} -alkyl or heteroaryl- C_{1-3} -alkyl groups, while the abovementioned phenyl groups and heteroaryl groups may in each case be substituted by one to three fluorine, chlorine or bromine atoms, by one to three C_{1-3} -alkyl groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, by one to three hydroxy groups, one to three C_{1-3} -alkoxy groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or by a carboxy, C_{1-3} -alkoxycarbonyl, aminocarbonyl, C_{1-3} -alkylaminocarbonyl, N,N-di- $(C_{1-3}$ -alkyl)-aminocarbonyl, N,N-di- $(C_{1-3}$ -alkyl)-amino, nitro or amino group, or

R_f and R_g together with the nitrogen atom between them denote a 3- to 7-membered cycloalkyleneimino group, while the methylene group in the 4 position of a 6- or 7-membered cycloalkyleneimino group may additionally be replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N- $(C_{1-3}$ -alkyl)-imino group,

while the tricyclic group in the abovementioned general formula I may be mono- or disubstituted by fluorine or chlorine atoms, by methyl or methoxy groups and the substituents may be identical or different,

and by the abovementioned heteroaryl groups are meant 6-membered heteroaryl groups containing one, two or three nitrogen atoms, or 5-membered heteroaryl groups which may contain one to four heteroatoms such as, for example, nitrogen, oxygen and sulphur, while hydrogen atoms bound to nitrogen may optionally be replaced by C_{1-3} -alkyl groups,

the isomers and the salts thereof.

2. Substituted piperazine derivatives of general formula I according to claim 1, wherein

n denotes the number 3, 4 or 5,

m denotes the number 2 or 3,

X denotes a carbon-carbon bond, an oxygen atom, a methylene, ethylene, imino or N-(C₁₋₃-alkyl)-imino group,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R₁ and R₂, wherein

R₁ denotes a hydrogen, fluorine, chlorine or bromine atom, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a hydroxy group, a C₁₋₄-alkoxy group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a phenoxy, heteroaryloxy, phenyl-C₁₋₃-alkoxy, carboxy, C₁₋₃-alkoxycarbonyl, aminocarbonyl, C₁₋₃-alkylaminocarbonyl, N,N-di-(C₁₋₃-alkyl)-aminocarbonyl, nitro, amino, C₁₋₃-alkylamino, di-(C₁₋₃-alkyl)-amino, phenyl-C₁₋₃-alkyl-amino, N-(C₁₋₃-alkyl)-phenyl-C₁₋₃-alkylamino, C₁₋₃-alkylcarbonylamino, N-(C₁₋₃-alkyl)-C₁₋₃-alkyl-carbonylamino, C₁₋₃-alkylsulphonylamino or N-(C₁₋₃-alkyl)-C₁₋₃-alkylsulphonylamino group, while the abovementioned phenyl or heteroaryl moieties of the group R₁ may be substituted by one to five fluorine, chlorine or bromine atoms, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a hydroxy

group, or a C₁₋₄-alkoxy group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, and

R₂ denotes a hydrogen, fluorine, chlorine or bromine atom, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or a C₁₋₄-alkoxy group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or

R₁ and R₂ together represent a methylenedioxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl or monocyclic heteroaryl group, while the abovementioned phenyl groups and heteroaryl groups may in each case be substituted by a fluorine, chlorine or bromine atom, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, by a hydroxy, or C₁₋₃-alkoxy group,

R_b and R_c independently of one another denote a hydrogen atom or a C₁₋₃-alkyl group and

R_f and R_g, which may be identical or different, denote hydrogen atoms, C₁₋₆-alkyl groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, C₃₋₇-cycloalkyl groups, phenyl, heteroaryl, phenyl-C₁₋₃-alkyl or heteroaryl-C₁₋₃-alkyl groups, while the abovementioned phenyl groups and heteroaryl groups may in each case be substituted by one to three fluorine, chlorine or bromine atoms, by one to three C₁₋₃-alkyl groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, by one to three hydroxy groups, one to three C₁₋₃-alkoxy groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or

by a carboxy, C₁₋₃-alkoxycarbonyl, aminocarbonyl, C₁₋₃-alkylaminocarbonyl, N,N-di-(C₁₋₃-alkyl)-aminocarbonyl, N,N-di-(C₁₋₃-alkyl)-amino, nitro or amino group, or

R_f and R_g together with the nitrogen atom between them denote a 3- to 7-membered cycloalkyleneimino group, while the methylene group in the 4 position of a 6- or 7-membered cycloalkyleneimino group may additionally be replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N-(C₁₋₃-alkyl)-imino group,

the isomers and the salts thereof.

3. Substituted piperazine derivatives of general formula I according to claim 1, wherein

n denotes the number 3, 4 or 5,

m denotes the number 2 or 3,

X denotes a carbon-carbon bond or an oxygen atom,

R_a is defined as in claim 2, and

R_b and R_c independently of one another denote a hydrogen atom or a methyl group and

R_f denotes a hydrogen atom, a C₁₋₆-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a C₃₋₇-cycloalkyl group, phenyl, heteroaryl, phenyl-C₁₋₃-alkyl or heteroaryl-C₁₋₃-alkyl group, while the abovementioned phenyl groups and heteroaryl groups may in each case be substituted by one to three fluorine, chlorine or

- 59 -

bromine atoms, by one to three C₁₋₃-alkyl groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, by one to three hydroxy groups, one to three C₁₋₃-alkoxy groups wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, or by a nitro or amino group, and

R_g denotes a hydrogen atom,

the isomers and the salts thereof.

4. Substituted piperazine derivatives of general formula I according to claim 1, wherein

n denotes the number 4,

m denotes the number 2,

X denotes a carbon-carbon bond or an oxygen atom,

R_a denotes a phenyl group or heteroaryl group substituted by the groups R₁ and R₂, wherein

R₁ denotes a hydrogen, fluorine or chlorine atom, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a C₁₋₄-alkoxy group, a phenoxy group, a phenyl-C₁₋₃-alkoxy or a nitro or amino group,

wherein the abovementioned phenyl moiety of the phenoxy group may be substituted by a chlorine atom or by a methoxy group,

R₂ denotes a hydrogen atom, a chlorine atom or a C₁-C₄-alkoxy group,

or R_a denotes a monocyclic heteroaryl or phenyl group which is substituted in each case by a phenyl group,

R_b and R_c independently of one another denote a hydrogen atom or a C_{1-3} -alkyl group and

R_f denotes a C_1 - C_6 -alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a phenyl- C_{1-3} -alkyl group, while the abovementioned phenyl group may be substituted in each case by a fluorine atom or by a C_1 - C_3 -alkoxy group, and

R_g denotes a hydrogen atom,

the isomers and the salts thereof.

5. The following substituted piperazine derivatives of general formula I according to claim 1:

(a) 9-[4-(4-biphenyl-3-yl-piperazin-1-yl)-butyl]-9H-fluorene-9-carboxylic acid-(2,2,2-trifluoroethyl)-amide and

(b) 9-[4-(4-biphenyl-4-yl-piperazin-1-yl)-butyl]-9H-fluorene-9-carboxylic acid-(2,2,2-trifluoroethyl)-amide,

the isomers and the salts thereof.

6. Physiologically acceptable salts of the compounds according to claims 1 to 5.

- 61 -

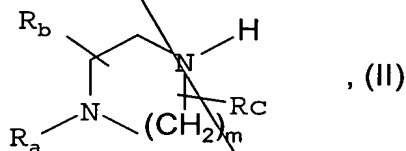
7. Medicaments, containing a compound according to at least one of claims 1 to 5 or a salt according to claim 6 optionally together with one or more inert carriers and/or diluents.

8. Use of a compound according to at least one of claims 1 to 5 or a salt according to claim 6 for the preparation of a medicament having a lowering effect on the plasma levels of atherogenic lipoproteins.

9. Process for preparing a medicament according to claim 6, characterised in that a compound according to at least one of claims 1 to 4 or a salt according to claim 5 is incorporated in one or more inert carriers and/or diluents by a non-chemical method.

10. Process for preparing the compounds according to claims 1 to 6, characterised in that

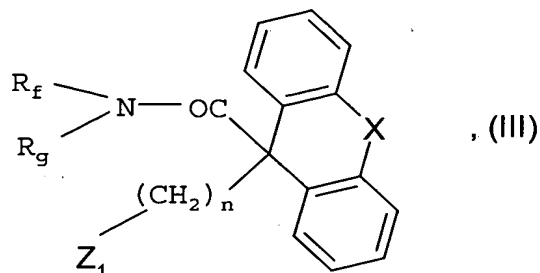
a. a compound of general formula



wherein

R_a , R_b and R_c are defined as in claims 1 to 4, is reacted with a compound of general formula

- 62 -

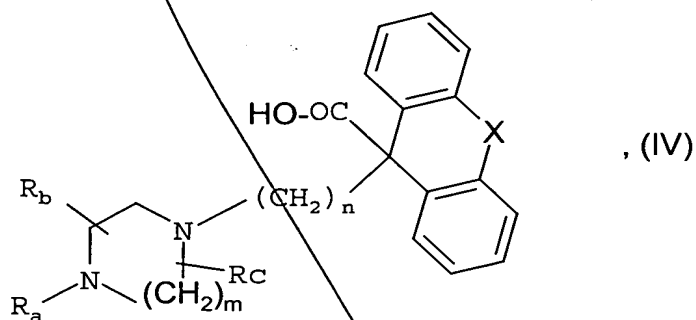


wherein

n , R_f , R_g and the tricyclic system are defined as in claims 1 to 4 and

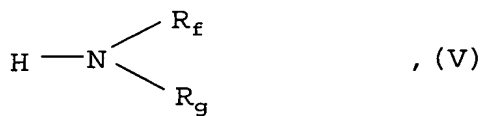
Z_1 denotes a nucleofugic leaving group, or

b. a compound of general formula



wherein

the tricyclic system is defined as in claims 1 to 4, is reacted with an amine of general formula



- 63 -

wherein

R_f and R_g are defined as in claims 1 to 4, or with the reactive derivatives thereof and

if desired a compound of general formula I thus obtained which contains a nitro group is converted by reduction into a corresponding amino compound and/or

a compound of general formula I thus obtained wherein R_f denotes a hydrogen atom is converted by alkylation into a corresponding compound wherein R_f denotes a C_{1-3} -alkyl or phenyl- C_{1-3} -alkyl group and/or

any protecting group using to protect reactive groups during the reactions is cleaved and/or

a compound of general formula I thus obtained is resolved into its stereoisomers and/or

a compound of general formula I thus obtained is converted into the salts thereof, particularly for pharmaceutical use into the physiologically acceptable salts thereof with an inorganic or organic acid or base.

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